IV. REMARKS

Claims 21-27 are pending.

37 CFR 1.52

The specification is objected to under 37 CFR 1.52. Specifically, pages 17-18 have tables that extend beyond the limits required for margins, which has resulted in punch hole obliteration of the right edge of Table 2.

Pursuant to the examiner's request, substitute pages 17 and 18 are submitted herewith.

35 U.S.C. 112, second paragraph

Claims 21-27 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

To obviate this rejection, claim 21 has been amended to include the limitations of non-elected base claim 1.

The examiner has rejected claims 22-27 as each being unclear in line 1 by reciting "the mammal". These claims have been amended to clarify that the composition is being administered to the mammal being treated.

Claims 22-27 are rejected as being unclear by reciting "canine species", "bovine species" etc. the examiner states that each of the recited members is a "Family", not a "species", according to the classification system of Linnaeus.

Applicant thanks the examiner for pointing out the error in nomenclature and has revised the references in the claims accordingly.

35 U.S.C. 101

Claims 21-27 stand rejected under 35 U.S.C. 101 because, as stated by the examiner, the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. The examiner states that claims 21-27 provide for the use of a composition of blood components but do not set forth any steps

involved in the method/process, and that a claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Applicant traverses the rejection. The claims do recite an active step. The active step involved is the administration of a physiologically effective dose.

35 U.S.C. 103 (a)

Claim 21

Claim 21 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Thorbecke et at. (4,702,808), as evidenced by Maione et al. (5,086,164) and in view of Nagai et at. (5,464,816).

In the office action the examiner states that Thorbecke et al. teach the use of whole human serum containing the immunostimulating polypeptide platelet factor 4 (PF4) to treat immunosuppressed mice, referring to col. 3, lines 53-57, col. 4, lines 11-12 and Examples 2-4 and 6. The examiner notes that PF4 is a polypeptide inherently having molecular weight of about 7,800 daltons, as evidenced by Maione et al. at col. 2, lines 19-26 and thus falls within applicant's claimed limit of 60,000 daltons and within applicant's further disclosed limit of 8,000 daltons.

The examiner also states Nagai et al. teach that mammalian sera contain a nonapeptide (ca. 1000 daltons) designated as serum thymic factor (FTS) which has immunostimulating activity and which can be used to treat immunodeficiencies as discussed at col. 2, lines 10-30 and col. 3, lines 2-17.

Applicants traverse this rejection.

What Thorbecke teaches is the use of PF4 as an immunomodulator and provides a method of obtaining PF4 from platelet releasate. In the portion of the reference referred to by the examiner, Thorbecke states that "Although any PF4-containing preparation (normal serum, or platelet releasate) can be used to modulate immune response, it is preferable to use purified PF4 preparations." Thorbecke discloses the use of whole serum or platelet releasate; Thorbecke does not mention utilizing a portion of normal serum, where the portion is selected on a molecular weight basis.

Unlike Thorbecke, Nagai does not mention the use of whole serum, let alone a specific portion of whole serum. On the contrary, Nagai cautions against using serum compounds having a molecular weights higher than that of FTS [approx. 1000 daltons][col. 4, lines 33-45]. Applicants claimed serum portion contains serum components having molecular weights of up to 8000 daltons.

Thus, Nagai specifically teaches away from applicants composition.

As stated by the examiner, Nagai does disclose a pharmaceutical composition containing serum thymic factor (FTS). But Nagai's pharmaceutical composition is limited to purified or synthetic FTS, not to a serum fraction containing FTS in conjunction with a multitude of other immunomodulators.

The examiner argues that since low molecular weight immunostimulating polypeptides such as the PF4 of Thorbecke et al. and the FTS of Nagai et al. were known to exist in mammalian serum, it would have been obvious to obtain a low molecular weight fraction (e.g. with a cut-off M. W. of 8000 daltons), in lieu of whole serum, for the therapeutic administration of these polypeptides. Applicant points out that its current presented claims are directed to fractions having a cut-off of 60,000 daltons, not 8,000 daltons [its preferred compositions have a cut-off of 8,000 daltons].

On pages 2 to 4 of the specification, applicant acknowledges and discusses the work being done on bio-active peptides such as those discussed in applicant's specification or by Nagai or Thorbecke. But neither the work referred to in the specification or by Thorbecke or Nagai discloses or suggests the use of naturally occurring peptides and other components synergistically working to modulate immune behavior through the many different pathways by which the myriad of serum components act. In these references, the direction is toward purified components acting alone, not to the use of the naturally occurring combination claimed by applicant.

The examiner argues that motivation to use such a low molecular weight fraction comes from the fact that it is known that whole serum contains numerous high molecular weight proteins, which would induce undesired immune responses in the treated mammal as, for example, specified by Nagai et al. at col. 4, lines 41-45.

A closer inspection of this reference in Nagai is needed here. Nagai states that such "high molecular weight proteins, which would induce undesired immune responses"

are "of a higher molecular weight compared to FTS ..." [col. 4, lines 42-44]. Since Nagai's FTS has a molecular weight of approx. 1000 daltons, this teaching leads directly away from combining Nagai's FTS with Thorbecke's PF4 [7800 daltons] or with any of the multitude of other components present in applicants serum fraction. Not only does Nagai specifically teach away from using Thorbecke's 7,800 dalton peptide, it unquestionably teaches away from applicant's currently presented claims directed to a 60,000 dalton fraction.

In other words, the text of Nagai 1] does not allow the combination of his teaching with that of Thorbecke, and 2] teaches away from a fraction having a cut-off of 8,000 daltons, and certainly one with a cut-off of 60,000 daltons.

The examiner further states that one would have been motivated to administer the peptide components across species (to prevent xenogeneic responses). But once again, this is directly refuted by Nagai who states, again referring to high molecular weight components [over 1000 daltons], at col. 4, lines 44-45, "where they are of non-human origin, they may give rise to allergic or anaphylactic developments". The data presented in applicant's specification demonstrates that in fact, applicant's composition can work well across species.

The examiner also states that, by administering a fraction of serum containing low molecular weight polypeptides, one would have expected that one would gain the advantage of administering more than one immunostimulating polypeptide -e.g. one would thus administer both the PF4 of Thorbecke et al. and the FTS of Nagai et al. and thereby achieve at least two immunoenhancing effects. But this is directly contrary to the teaching of the references – Nagai states [see above] they cannot be combined as the examiner suggests.

In summary, the Thorbecke and Nagai references cannot be combined because of the teachings set forth in the text of these references. Even if they could be combined , at best they show or suggest the combination of two distinct purified peptides, not a fraction of serum containing multiple active peptides and other components acting in a naturally synergistic relationship with that multitude of peptides.

Claims 22-24 and 27

Claims 22-24 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thorbecke et al. in view of Nagai et al. as applied to claim 21 above, and further in view of Ansley 5,219,578.

Thorbecke et al. and Nagai et al. have been cited for the obviousness of administering a fraction of serum containing low molecular weight polypeptides in order to provide an immunostimulating treatment. The examiner states that it would have reasonably expected that such treatment would enable a mammal to show enhanced immunoresponsiveness to numerous known infectious agents to which it is commonly exposed. Ansley shows that it is of interest to immunostimulate canines again parvovirus (Example 7) as in instant claims 22-23, bovines against shipping fever (Example 5) as in instant claim 24, and equines against lower respiratory disease, as in instant claim 27. Note that "respiratory infection" encompasses what Ansley teaches and that "lower airway disease" is understood to be the same as "lower respiratory disease" of Ansley. The limitations of dependent claims 22-24 and 27 thus would have been obvious.

Applicants traverse this rejection. The impropriety of combining the Thorbecke and Nagai et al. references is discussed above. The primary basis for lack of obviousness with regard to these claims resides not in the specific disease for which applicants composition is used but in the use of the composition in general for immunomodulation with respect to any challenge.

Claims 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thorbecke et al. in view of Nagai et al. as applied to claim 21 above, and further in view of Fraser et al. (Merck Veterinary Manual).

Thorbecke et al. and Nagai et al. have been cited for the obviousness of administering a fraction of serum containing low molecular weight polypeptides in order to provide an immunostimulating treatment. The examiner states that it would have reasonably expected that such treatment would enable a mammal to show enhanced immunoresponsiveness to known infectious agents to which it is commonly exposed.

Regarding claims 22-23, the examiner states Fraser et al. teach (pages 249-250) that parvoviral infections are a known disease of canines; that any low molecular weight fraction of serum would contain balanced salts as well as low molecular weight peptides. Administration of such a salt balanced fluid would provide the fluid therapy taught by

Fraser et al. (para. spanning pages 249-250) and that, since Thorbecke et al. teach use ofPF4 as an adjuvant (col. 5, lines 11-19), one would have been motivated to use such as an adjuvant in the immunization treatments taught by Fraser et al. (Page 250).

Regarding claim 24, the examiner states Fraser et al. teach shipping fever as a known disease affecting bovines (pages 723-724); immunizations (page 724, third para.); and, as argued above regarding claims 22-23, provision of serum PF4 as an adjuvant would have been obvious for immunizations.

With respect to claim 25, the examiner states Fraser et al. teach enteritis as a type of disease known in porcines (pages 195-197) and maintaining hydration and immunization (page 197, third para.). the examiner also states that, as noted supra for claims 22-23, administration low molecular weight serum would provide for hydration and it would provide an adjuvant for immunization.

Applicant traverses these rejections since applicant is neither vaccinating nor immunizing a mammal but merely modulating its immune behavior either before or after challenge. Any hydrating effect of applicants composition is merely a by-product of its use.

Regarding claim 26, Fraser et al. teach (page 39) that Feline leukemia virus causes immunosuppression. Thus, the examiner argues, it would have been obvious to employ an immunostimulating serum composition containing PF4 of Thorbecke et al. and FTS of Nagai et al. to treat this condition in felines.

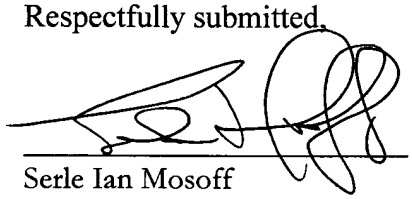
With respect to claim 27 Fraser et al. teach (pages 854-855) that equines can develop warts (papillomas) and that vaccination can be used to control the disease in herds. Since Thorbecke et al. teach use of serum PF 4 as an adjuvant in vaccinations/immunizations, the examiner argues it would have been obvious to employ such an adjuvant in the immunizations taught by Fraser et al.

Applicant traverses this rejection since applicant is neither vaccinating or immunizing mammal but merely modulating their immune behavior either before or after challenge.

SUMMARY & CONCLUSION

In view of the above discussion of the issues and amendment of the claims, applicant respectfully submits that the claims are in condition for allowance. Favorable reconsideration and allowance of the claims are respectfully requested. If the claims are not yet found to be in condition for allowance, for any reason, the Examiner is respectfully requested to telephone the undersigned at (212) 940-8717, to discuss the subject application and/or to identify a time at which a personal interview would be granted.

Respectfully submitted,



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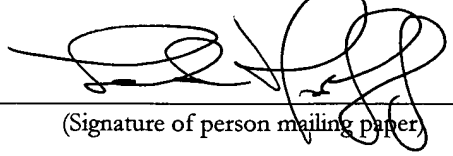

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